

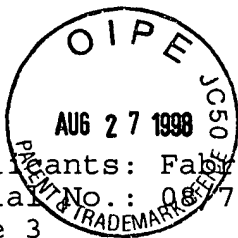
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Rejection under 35 U.S.C. §103(a)

In the March 19, 1998 Advisory Action, the Examiner maintained the rejection of claims 1 and 3-10 as obvious over Hershenson. The Examiner stated that Hershenson suggests that mannitol or HSA, alone or in combination, would reasonably be expected to stabilize IFN- β in the absence as well as the presence of glycerol or PEG. The Examiner acknowledged that Hershenson is silent on the use of formulations which lack glycerol or PEG but still maintained that the reference provides no evidence which teaches that IFN- β would not be stable absent such components.

In response, applicants respectfully traverse the Examiner's rejection. Applicants submit herewith a Rule 132 Declaration by Dr. Pierandrea Esposito in support of their position as discussed below. As the Examiner has recognized, this reference teaches that a stabilizing amount of either glycerol or polyethylene glycol (PEG) must be present and applicants maintain that there is nothing in the reference which suggest that other materials (such as mannitol) can function as a stabilizer **in the absence** of either glycerol or PEG. It is respectfully pointed out that silence in a reference is an inadequate disclosure of facts upon which a conclusion of obviousness may justifiably follow. In re Burt, 148 USPQ 548 (CCPA 1966); In re Newell, 13 USPQ2d 1248, 1250 (Fed. Cir. 1989).

Furthermore, applicants maintain that Hershenson's teachings are based on the generally known fact polyethylene glycols and glycerol are commonly used chemically stable vehicles in the liquid formulation of stable parenteral dosage forms. As further evidence of the unobviousness of using mannitol alone to stabilize INF- β , the Examiner is directed to Tables 4 and 5 of the specification on pages 10 and 11 where it can be noticed that the compounds commonly used in the art as "stabilizers" (such as



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mannitol, sucrose and glycine) have different effect on the stability of INF- β . Therefore, one cannot predict the stabilizing effect of any of these agents alone on any particular protein without testing it beforehand.

In addition, applicants point out that the use of acetate buffer (as specified in claim 5) brings in additional unexpected stabilization results when compared with other buffers such as citrate, ascorbate and succinate (see specification on pages 7-9, Tables 1-3). There is nothing in the prior art that discloses or suggest that the use of citrate buffer along with mannitol brings additional stabilizing effect to INF- β ,

In light of the foregoing, it is respectfully submitted that this application is now in condition to be allowed and the early issuance of a Notice of Allowance is respectfully solicited.

EXPRESS MAIL CERTIFICATE

I hereby certify that this correspondence is being deposited with the United States Postal Service as Express Mail Post Office to Addressee (mail label #EH393852735US) in an envelope addressed to: Assistant Commissioner for Patents, Box CPA, Washington, D.C. 20231, on August 27, 1998
Dorothy Jenkins

Name of Person Mailing Correspondence .

Dorothy Jenkins

Signature

August 27, 1998

Date of Signature

EAM:CCA:lac

Respectfully submitted,

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